Claims

1. A method to prepare living cells which cells comprise a first fluorescent protein localized to the nucleus and a second fluorescent protein localized to the cytoplasm

wherein said first and second fluorescent proteins emit light of different wavelengths which method comprises

modifying living cells to contain either

(a) a first expression system for expression of said first fluorescent protein wherein said first fluorescent protein is fused to an amino acid sequence which targets said fusion protein to the nucleus and a second expression system for expression of a second fluorescent protein lacking a nucleus targeting sequence; or

(b) an expression system that expresses both said first fluorescent protein and second fluorescent protein as described; and

selecting said modified cells for cells that have been stably modified.

2. The method of claim 1, wherein in step (a), said cells are first modified with said first expression system and then modified with said second expression system or *vice versa*.

3. The method of claim 1, wherein in step (a), the cells are modified with both expression systems simultaneously.

4. The method of claim 1, wherein said selecting is by culturing in the presence of an antibiotic or a toxin.

5. Living cells stably modified to produce a first fluorescent protein fused to an amino acid sequence targeting the nucleus and a second fluorescent protein lacking an amino acid sequence targeting the nucleus;

wherein said first and second fluorescent proteins emit visible light at different wavelengths.

6. Living cells which are modified to contain a first fluorescent protein localized to the nucleus and a second fluorescent protein localized to the cytoplasm wherein said first fluorescent protein and second fluorescent protein are of different colors.

7. The cells of claim 6, wherein said first fluorescent protein is green and said second fluorescent protein is red.

8. The cells of claim 5, wherein said amino acid sequence targeting the nucleus is histone H2B.

9. A method to determine the cell cycle position of living cells which method comprises assessing the ratio of nuclear area to cytoplasmic area of the cells of claim 6.

10. The method of claim 9, wherein said assessing is performed as a function of time.

11. The method of claim 9, wherein said cells are observed in a living animal.

12. A method to determine the effect of an agent on cells, which method comprises

treating a first sample of the cells of claim 6 with said agent and observing the effect of said treating on the distribution and/or intensity of radiation emitted from said cells.

13. The method of claim 12, which further comprises observing the distribution and/or intensity of radiation emitted from said cells that have not been treated with said agent, and

comparing the observations made on the first sample with those on the second sample.

14. The method of claim 12, wherein the distribution and/or intensity are characteristic of dormancy.

15. The method of claim 12, wherein said distribution and/or intensity are characteristic of apoptosis.

16. The method of claim 12, wherein said distribution and/or intensity are characteristic of stages in the cell cycle.

17. A method to determine the location of targeting of an agent which method comprises treating the cells of claim 6 with said agent and observing the distribution and/or intensity of radiation emitted from said cells.

18. The method of claim 17, wherein said agent itself is labeled, and said method further comprises directly observing the location of the label.

19. A method to determine the proliferation rate of a cell culture which method comprises culturing cells which have been modified to contain a fluorescent protein; and

measuring the fluorescence emitted by said cells as a function of time,

whereby the rate of proliferation of said cells is determined.

20. The method of claim 19, wherein said fluorescent protein is a green fluorescent protein (GFP) or a red fluorescent protein (RFP).

21. The method of claim 19, wherein said culture is grown from a single cell.

22. A method to determine the effect of a test compound on cell proliferation which method comprises

culturing cells in the presence and absence of said test compound, wherein said cells have been modified to contain a fluorescent protein;

measuring the intensity of fluorescence as a function of time in the presence and absence of said compound so as to determine the rate of proliferation in the presence and absence of said compound; and

comparing the rate of proliferation in the presence and absence of said compound;

wherein a change in the rate of proliferation in the presence as opposed to the absence of said compound identifies said compound as a modulator of cellular proliferation.

23. The method of claim 22, wherein said fluorescent protein is a green fluorescent protein (GFP) or a red fluorescent protein (RFP).

24. The method of claim 22, wherein said culturing is commenced from a single cell.

25. A method to determine the heterogeneity of a tumor, which method comprises culturing a multiplicity of colonies from individual cells or individual groups of cells contained in said tumor; and

determining the rates of proliferation of said cell cultures;

whereby cultures exhibiting different rates of proliferation indicate heterogeneity of said tumor.

26. The method of claim 25, wherein said cells have been modified to contain a fluorescent protein and the rates of proliferation are determined by measuring the intensity of emitted fluorescence as a function of time.

27. The method of claim 25, wherein said cells have been modified to contain a first fluorescent protein localized to the nucleus and a second fluorescent protein localized to the cytoplasm wherein said first fluorescent protein and second fluorescent protein are of different colors.